REMARKS

These remarks are in response to the Office Action mailed March 30, 2004. Claim 1 has been amended to more particularly define Applicants' invention. Thus, the amendment introduces no new matter. Claims 1-15 are pending, of which claims 1-3, 5 and 6 are currently under consideration.

A. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 5, and 6 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The rejection is respectfully traversed.

With regard to the term "combining" as recited in Claim 1 (item 15 on page 5 of the Office Action), this term is clear and unambiguous. Claim 1, as amended, recites:

> "separating the proteomic mixture into two portions, treating one of the two portions with the candidate compound to obtain an inactivated portion, wherein the candidate compound is a non-covalent agent, combining at least one probe with the untreated portion of said mixture under conditions for reaction with said target proteins to obtain a first specimen, combining at least one probe with the inactivated portion under conditions for reaction with said target proteins to obtain a second specimen"

It is respectfully submitted that every limitation recited above particularly points out and distinctly claims the subject matter which the Applicants regard as the invention.

With regard to the omission of a method step in Claim 1 (item 16 on page 5 of the Office Action), Applicants respectfully disagree that the method is incomplete. According to

the Examiner, essential steps have been allegedly omitted. However, the method of Claim 1 recites "... comparing the amount of each of the proteins separated from the first specimen and the second specimen **as indicative of the bioactivity** of said candidate compound with said target proteins."

To elaborate, claim 1 now recites that a "candidate compound" is a "non-covalent agent." The method recited in claim 1 compares the level of probe reactivity with the target proteins in the presence and absence of such non-covalent candidate compound. Differences in probe reactivity observed in the presence or absence of the non-covalent candidate compound are indicative of bio-activity of the candidate compound.

The Examiner suggested to add these steps: adding the probe to the sample followed by its reaction with the target protein. Yet, in view of the clarification that the candidate compound is a non-covalent agent, those having ordinary skill in the art recognize that the steps suggested by the Examiner are not required to practice the invention, because it is the comparison that correlates the bioactivity of a probe with the target protein. Thus, the method at issue is complete as currently presented. No additional steps are required.

For the reasons set forth above, it is respectfully submitted that the rejections of claims 1-3, 5, and 6 under 35 U.S.C. § 112, second paragraph, do not apply. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Rejection Under 35 U.S.C. § 103(a)

Claims 1, 2, 5, and 6 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over U.S. patent No. 6,391,649 to Chait et al. and Liu et al. (*PNAS*, 1999, 96(26):14694-14699). This rejection is respectfully traversed on the following grounds.

Claim 1 of the present invention, as currently amended, recites a method for screening for the bioactivity that includes

> "treating one of the two portions with the candidate compound to obtain an inactivated portion, wherein the candidate compound is a non-covalent agent, combining at least one probe with the untreated portion of said mixture under conditions for reaction with said target proteins to obtain a first specimen, combining at least one probe with the inactivated portion under conditions for reaction with said target proteins to obtain a second specimen"

Chait et al. do not disclose that they use "a non-covalent agent to obtain an inactivated portion" of the mixture. There is no indication Chait et al. have any "inactivated portion" at all, much less that they used non-covalent agents to prepare such portion. Indeed, a candidate compound is "a non-covalent agent," as recited in claim 1. The purpose of Chait et al.'s method is to determine the amount of protein in the mixture. However, protein levels do not change in response to a non-covalent agent. Clearly, Chait et al. had no need to use any non-covalent agents, and, consequently, they did not employ any.

Claim 1 also recites

> "employing at least one probe, ... comprising a reactive functionality group specific for said group of target proteins and a ligand."

Chait et al. fail to teach using such reactive probe with an untreated portion of the mixture.

Furthermore, the method recited in Claim 1 includes

> "comparing the amount of each of the proteins ... as indicative of the bioactivity of said candidate compound with said target proteins."

Thus, Claim 1 recites variations in protein **activity**, rather than just the quantity of protein expressed in a cell. Chait et al. are not concerned with the variations in protein activity, and are accordingly silent on the subject. As pointed out above, their teachings are directed solely to the analytical technique of determining the amount of protein, for example, using

mass spectroscopy. The Examiner clearly recognized this fact and stated (item 19, page 6 of the Office Action) that that Chait et al. "disclosed a method for accurately comparing the levels of ... proteins ..." Indeed, Chait et al. teach nothing else.

Accordingly, it is respectfully submitted that Chait et el. do not to teach or suggest every element of Claim 1. Liu et al. fail to cure the deficiencies of Chait et al. As correctly recognized by the Examiner, Liu et al. teach that fluorophosphonate-biotin can be used for activity-based protein profiling. This is all that is disclosed by Liu et al. There are no teachings in Liu et al. providing for the above-discussed elements of Claim 1 that are missing from Chait et al.

In view of the foregoing, it is submitted that Claim 1 is patentably distinguishable over the references cited by the Examiner, and is, therefore, allowable. Claims 2, 5, and 6 all depend on claim 1 and are allowable for at least the same reason. Accordingly, reconsideration and withdrawal of the rejection of claims 1, 2, 5, and 6 under 35 U.S.C. § 103(a) are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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